REMARKS

In response to the Communication from the Examiner mailed February 12, 2002, Applicants submit herewith a Sequence Listing in both paper and computer-readable forms in compliance with 37 C.F.R. §§1.821-1.825. The amendments specified above are made to include SEQ ID NOs that correspond to the sequence identifiers in the accompanying sequence listing. The amendments add no new matter.

Applicants hereby state that the sequences in the Sequence Listing are fully supported in the specification and therefore add no new matter. Further, Applicants state that the accompanying paper and computer-readable forms of the Sequence Listing are identical.

Respectfully submitted,

April 10, 2002
Date

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Version of amendments marked to show changes:

· On page 6, replace the paragraph at lines 22 to 27 with the following replacement paragraph:

-- **Figure 2:** Polynucleotide and polypeptide sequences (SEQ ID NOs 1 and 2, respectively) [Sequence] of the scFv that forms the basis of a library according to the invention. There are currently two versions of the library: a "primary" library wherein 18 positions are varied and a "somatic" library wherein 12 positions are varied. The six loop regions H1, H2, H3, L1, L2 and L3 are indicated. CDR regions as defined by Kabat (Kabat et al. (1991). *Sequences of proteins of immunological interest*, U.S. Department of Health and Human Services) are underlined.--

· On page 6 to page 7, replace the paragraph starting at page 6, line 35 and ending on page 7, line 2 with the following replacement paragraph:

-- **Figure 4:** Sequences of clones selected from libraries according to the invention, after panning with bovine ubiquitin (SEQ ID NOs: 7-18), rat BIP (SEQ ID NOs: 19-42), bovine histone (SEQ ID NOs: 43-96), NIP-BSA (SEQ ID NOs: 97-150), FITC-BSA (SEQ ID NOs: 151-198), human leptin (SEQ ID NOs: 199-222), human thyroglobulin (SEQ ID NOs: 223-240), BSA (SEQ ID NOs: 241-276), hen egg lysozyme (SEQ ID NOs: 277-288), mouse IgG (SEQ ID NO: 289-300) and human IgG (SEQ ID NOs: 301-318). Underlines in the sequences indicate the positions which were varied in the respective libraries.--

- On page 24, replace the paragraph at lines 22 to 27 with the following replacement paragraph:

-- Since it is preferable to mimic this distribution of amino acids, the invention provides a library wherein the distribution of amino acids at the positions to be varied mimics that seen in the antigen binding site of antibodies. Such bias in the substitution of amino acids that permits selection of certain polypeptides (not just antibody polypeptides) against a range of target ligands is easily applied to any polypeptide repertoire according to the invention. There are various methods of biasing the amino acid distribution at the position to be varied (including the use of tri-nucleotide mutagenesis, WO97/08320, Morphosys, supra), of which the preferred method, due to ease of synthesis, is the use of conventional degenerate codons. By comparing the amino acid profile encoded by all combinations of degenerate codons (with single, double, triple and quadruple degeneracy in equal ratios at each position) with the natural amino acid use it is possible to calculate the most representative codon. The codons (AGT)(AGC)T (SEQ ID NO: 3), (AGT)(AGC)C (SEQ ID NO: 4) and (AGT)(AGC)(CT) (SEQ ID NO: 5)– that is, DVT, DVC AND DVY, respectively using IUPAC nomenclature – are those closest to the desired amino acid profile: they encode 22% serine and 11% tyrosine, asparagine, glycine, alanine, aspartate, threonine and cysteine. Preferably, therefore, libraries are constructed using either the DVT, DVC or DVY codon at each of the diversified positions.--

· On page 24, replace the paragraph on lines 25 to 36 with the following replacement paragraph:

-- As stated above, polypeptides which make up antibody libraries according to the invention may be whole antibodies or fragments thereof, such as Fab, $F(ab')_2$, Fv or scFv fragments, or separate V_H or V_L domains, any of which is either modified or unmodified. Of these, single-chain Fv fragments, or scFvs, are of particular use. ScFv fragments, as well as other antibody polypeptides, are reliably generated by antibody engineering methods well known in the art. The

scFv is formed by connecting the V_H and V_L genes using an oligonucleotide that encodes an appropriately designed linker peptide, such as $(Gly\text{-}Gly\text{-}Gly\text{-}Gly\text{-}Ser)_3$ (SEQ ID NO: 6) or equivalent linker peptide(s). The linker bridges the C-terminal end of the first V region and N-terminal end of the second V region, ordered as either V_H-linker-V_L or V_L-linker-V_H. In principle, the binding site of the scFv can faithfully reproduce the specificity of the corresponding whole antibody and vice-versa.--

· On pages 48-50, replace Table 1 with the following replacement Table 1: